Re: Libby Epidemiology Action Plan Funding Request

Prepared by Aubrey Miller, MD, MPH

11/15/2007

Request per Doug Ammon
For Libby Action Plan Projects, I would like the following information each of the Task Leaders by COB Monday (although sooner would be better):

- Briefing Description (see attached descriptions)
- Date for Completion
- Next Major Milestone (e.g.,complete work plan, work product to peer review)
- Critical Information From Other Libby Action Plan Projects
- Other Potential Coordination Issues
- Potential Schedule Issues
- Potential Funding Needs (beyond current budget) (see attached spreadsheet for current budget info)

*The NHEERL projects, Analytical studies, and epi. studies can be "lumped" together.

I. Summary of Epidemiology Action Plan Studies & Activities:

During early 2007 Agency representatives began efforts to determine and outline the toxicity studies necessary to support the Libby BRA. While this early effort was primarily focused on animal toxicity studies and in-vitro investigations, several areas for epidemiologic research were also identified for consideration. Needed areas of epidemiologic research included: a) detailed characterization of health effects over time associated with exposure to Libby amphibole in groups of concern such as workers, those with childhood exposure, non-workers, susceptible populations etc., b) improved understanding of critical effects (both pulmonary and non-pulmonary) to support the site-specific RfC, c) data regarding individuals with low-level, long-term and short-term exposures and the development of disease, and d) longitudinal efficacy of clean-up actions in reducing health effects in the population.

A few general areas of epidemiologic research were subsequently included in the Libby Action Plan and received preliminary funding allocations to initiate needed work and pilot investigations:

a) ***Libby Amphibole RfC Development.*** Dr. Robert Benson with Region 8 is developing a site-specific RfC (the non-cancer toxicity value) for Libby Amphibole based primarily on epidemiological information from the Marysville, Ohio cohort who were exposed to Libby Amphibole. NCEA will assist by evaluate options for quantitative analysis of the Marysville, Ohio cohort including additional statistical support. Additionally, a human dosimetry model, constructed by ORD/NHEERL, will be used to predict internal dose and will be integrated into the site-specific RfC. This site-specific product will be subject to external peer review. NCEA will provide assistance with the peer review process.
Funding: **2007: no funding; 2008: $25,000; 2009: $75,000 (Total $100,000)**

b) ***Libby Amphibole Cancer Assessment.*** ORD/NCEA will conduct a cancer assessment specifically for Libby Amphibole for the Integrated Risk Information System (IRIS). As with all IRIS assessments, available studies (epidemiologic and animal toxicity) will be considered, as well as models both for dosimetry and risk assessment. This effort will go through Agency and Interagency review as a standard assessment for the EPA's Integrated Risk Information System (IRIS).
Funding: **2007: no funding; 2008: $365,000 (Total $365,000)**

j) ***New Epidemiologic Information from Libby Montana Cohort.*** The Region 8 Technical Team and NCEA will review recently available WR Grace information concerning historical

worker asbestos exposures and associated asbestos-related abnormalities (pleural plaques, diffuse pleural thickening, asbestosis). This information will be included in the ongoing and future NIOSH cohort updates and may include extended morbidity investigation of former WR Grace workers to evaluate the exposure-response relationship; review and incorporate NIOSH mortality information; and evaluate biomarker data. Additionally, lung tissue collection will be pursued to improve the understanding of Libby Amphibole exposure and lung fiber deposition dosimetry and to support exposure-response modeling.
Funding: **2007: $511,648; 2008: $185,000 (Total $696,648)**

k) ***New Epidemiologic Information from Other Cohorts.*** NCEA and Region 8 will work with NIOSH and ATSDR to develop epidemiologic information from other cohorts exposed to Libby Amphibole.
Funding: 2007: $250,000; 2008: $250,000 (Total $500,000)

On July 23-24, 2007, a meeting was held in Denver with experts directly knowledgeable about the Libby situation and asbestos-related epidemiologic research. Participants included individuals from ATSDR, NIOSH, EPA, Libby Center for Asbestos Related Diseases, Libby community technical group representatives, Karmanos Cancer Institute, Mt. Sinai Hospital, University of Cincinnati, and University of Montana. The goal of the meeting was to provide input into the development of a multi-year action plan for future epidemiologic studies and analyses (both historical and prospective) to support EPA's regional and national efforts to address the non-occupational risks associated with exposure to Libby Amphibole.

Critical objectives and areas of discussion focused on:

A. Potency of Libby Amphibole (LA) for both cancer & non-cancer lung disease.
Is the asbestos-related disease being experienced by individuals exposed to LA different (clinical course, severity, prognosis) from individuals exposed to other asbestiform mineral fibers ?

B. Identification of most susceptible populations compared to healthy workers.
Do individuals who are exposed in childhood or who have other illnesses (i.e., autoimmune disease, other pulmonary disease, other illnesses) have increased risk for asbestos-related disease in this population ?

C. Identification of any non-pulmonary critical health endpoints.
Are individuals in this population experiencing increased adverse-health effects secondary to LA exposure aside from asbestos-related pulmonary disease , if so, are such health effects more sensitive to exposure than pulmonary health endpoints?

D. Development of new exposure-response relationships for health endpoints of concern.
Can we better understand/characterize and quantify the historical exposure-response relationships in both occupationally and non-occupationally LA exposed individuals? Emphasis needs to be placed on risks associated with lower-level exposures and the development of scientifically sound inhalation reference concentration (RfC) and cancer-slope factors.

E. Improved understanding of the human toxicology associated with LA exposure.
How can we improve our understanding of *pulmonary fiber exposure* with respect to nature of fibers deposited in the lungs (i.e., morphologic and mineralogic characteristics), locations of deposition, pathology associated with deposition, and translocation to non-pulmonary tissues.

During the meeting a number of activities and areas of epidemiologic research were identified and prioritized to some degree. A synopsis of the meeting discussions was circulated for comments and finalized for distribution on September 28, 2007 (see attached). Follow-up discussions were conducted with several meeting participants and groups, including a meeting last week in Atlanta with ATSDR

representatives, to evaluate specific activities and studies which could be conducted to support EPA's needs. Information provided from all the meetings and discussions were used to develop a tabular listing of the activities and potential studies to address the critical data-gaps needed for the Libby BRA (see attached). The current prioritization of projects was based on the following factors: 1) ability to accomplish project within 3 years, 2) perceived importance to BRA, 3) quality of data, if available, 4) perceived importance to the long-term needs of EPA and the Community, and 5) ability to support or enhance other research and investigations to the benefit of the community. The current prioritization is subject to change based upon identification of newer information or results from ongoing activities, input from others with differing needs or priorities, and essential temporal relationships between different projects (i.e., a functioning Libby Datasystem needs to be in place for certain projects to be viable). Project proposals and cost estimates for higher priority projects or investigations were also obtained (available on request).

II. Libby Epidemiology Action Plan Projects and Funding Request

1. Libby Amphibole RfC Development using Marysville Workers (previous funding need A).

Description: (High Priority)

New exposure data from OM Scott has been obtained and additional information has been requested to develop a more complete estimate of all worker exposures for use in the development of the RfC. Improved cost estimates have been obtained for this project based on the acquisition of new data and need to develop a new exposure matrix. Furthermore, there was strong consensus that improved health endpoints should be collected on the workers by University of Cincinnati researchers (i.e, CT scans and full pulmonary function testing) in order to obtain the most useful and robust response data possible for the RfC calculations. This is a high priority collaborative project between EPA R8, University of Cincinnati, and NCEA.

Costs:

* [redacted]

New Request in addition to previous funding for RfC development:

1) **Additional cost for RfC exposure matrix development: $ 71,600**
2) **New costs for acquisition of new health endpoints: $ 815,000**

Total New Costs for RfC development : $886,600

Milestones & Critical Actions:

- Awaiting funding commitments
- Prepare scope of work & contract between EPA R8 and Univ. of Cincinnati

Completion Date: *The project completion date is December 2009.*

2. Libby Amphibole Cancer Assessment (previous funding need B.).

Description: (High Priority)

ORD/NCEA will conduct a cancer assessment specifically for Libby Amphibole for the Integrated Risk Information System (IRIS). As with all IRIS assessments, available studies (epidemiologic and animal toxicity) will be considered, as well as models both for dosimetry and risk assessment. This effort will go through Agency and Interagency review as a standard assessment for the EPA's Integrated Risk Information System (IRIS). Priority high.

Costs:

[redacted]

Milestones & Critical Actions per NCEA

Completion Date: per NCEA

3. *New Epidemiologic Information from Libby Montana Cohort* [redacted].
Previous Funding Allocation: 2007: $511,648; 2008: $185,000 ([redacted]) **AND**
New Epidemiologic Information from Other Cohorts ([redacted]).
Previous Funding: 2007: $250,000; 2008: $250,000 ([redacted])
[redacted]

These activities/investigations and associated areas of funding need have been further subdivided into the critical research areas as follows:

a. **Development of CARD Clinic Data System & Enhance Utilization of all Clinical Datasets.**

Description: (High Priority)
Critical infrastructure development to enable epidemiologic research using clinical information collected on over 1200 individuals, acquisition of new data regarding critical EPA objectives (see above), and merging of other and new data-sets for analyses involving critical EPA objectives. EPA R8 is the lead, in collaboration with EPA ERT, and the CARD Clinic.

Costs:

Cost for development of CARD data system: $1,080,220

Milestones & Critical Actions:
- Awaiting funding commitments
- Needs assessments, data system hardware & software evaluations complete
- Need scope of work and contract with the CARD Clinic

Completion Date: *The project completion date is December 2009.*

b. **Follow-up collection of standardized health information and testing.**

Description: (High Priority)
New epidemiologic investigation of approximately 600 individuals selected to be consistent with EPA's critical objectives (i.e., exposure-response among low-exposure groups, clinical course of disease, susceptibility risk factors, non-pulmonary health endpoints, biomarkers for exposure and disease etc.). This investigation will entail the use of improved exposure questionnaires, acquisition of new health information, follow-up medical testing (i.e., X-rays, CT scan, full pulmonary function tests, immune profiles), and analyses utilizing all available clinical and exposure information to understand critical objectives in support of an EPA BRA. This will be a collaborative project between EPA, ATSDR, and the CARD.

Costs:

Cost for follow-up data & new epidemiologic study: $2,000,000*
(*includes 20% overhead for ATSDR)

Milestones & Critical Actions:
- Awaiting funding commitments
- Need scope of work and contract with the CARD Clinic for data acquisition
- Need IAG with ATSDR for technical assistance with protocol development, analyses, and reports.

Completion Date: *The project completion 2 years.*

c. **Evaluation of increased risks and health effects associated with childhood exposures.**

Description: (High Priority)

Perform follow-up evaluations of approximately 600 participants that were less than 18 years age during the 2000/2001. This investigation will entail the use of improved exposure questionnaires, acquisition of new health information, follow-up medical testing, and analyses utilizing all available clinical and exposure information to understand critical objectives, especially early-life exposures and effects, in support of an EPA BRA. Collaborative project between EPA, ATSDR, and the CARD. Can be combined with (b) above for additional cost savings.

Costs:

Cost for follow-up data & new study of early-life exposed group: $1,740,000*
(*includes 20% overhead for ATSDR)

Milestones & Critical Actions:

- Awaiting funding commitments
- Need scope of work and contract with the CARD Clinic for data acquisition
- Need IAG with ATSDR for technical assistance with protocol development, analyses, and reports.

Completion Date: *The project completion 2 years.*

d. **Compare clinical course of disease among Libby Amphibole exposed individuals to other asbestos exposed cohorts.**

Description: (High Priority)

Investigation to help determine specific health effects of Libby Amphibole (LA) exposures compared to other asbestos exposed populations. This investigation will evaluate the radiographic changes over time in plain radiographs (X-rays) and CT scans among differing exposure cohorts of interest. ATSDR has already evaluated the progression of radiographic changes among former Libby workers. This data can be readily compared to other worker cohorts to help understand if the clinical course of disease associated with LA exposure is different. Identified populations include Mt Sinai insulation workers, former textile workers exposed to chrysotile, Tyler, Texas, insulation workers exposed to amosite. Collaborative project between EPA R8, EPA NCEA, ATSDR, Mt Sinai, other exposed cohorts TBD. Estimated project completion 1 year.

Costs:

Cost for new study to evaluate clinical course of disease: $285,600*
(*includes 20% overhead for ATSDR)

Milestones & Critical Actions:

- Awaiting funding commitments
- Need IAG with ATSDR for technical assistance with protocol development, analyses, and reports.

Completion Date: *The project completion 1 year.*

e. Fiber tissue studies to support understanding of deposited fibers and associated pathology and lung dosimetry modeling of Libby Amphibole exposures.

Description: (Medium-High Priority)

Ongoing evaluation of lung tissue samples (surgical or post-mortem) for fiber burden & disease. Also, ongoing evaluation of fiber deposition, characterization, and pathology in post-mortem whole lungs specimens to specifically support the **EPA NHEERL dosimetry model development**. NHEERL requires approximately 25 cases x 15 fully characterized samples per case (per Anne Jarabek). Collaborative project between EPA R8, EPA NHEERL, Libby CARD Clinic, and identified centers with cohorts of interest.

Costs:

Est. Cost for fiber burden & lung dosimetry modeling study: $1,412,500*

(*costs may likely be lower with volume cost breaks, improved efficiencies, and actual availability of samples from each case)

Milestones & Critical Actions:

- Awaiting funding commitments
- Protocol development and IRB approvals
- Need scope of work and contract with the CARD Clinic and the analytical labs

Completion Date: *The project completion 3 years.*

Funding Summary for Libby Epidemiology Action Plan

Updated cost estimates under funding needs J & K

• Cost for development of CARD data system:	$1,080,220
• Cost for follow-up data & new study of critical Libby cohort:	$2,000,000
• Cost for follow-up data & new study of early-life exposed group:	$1,740,000
• Cost for new study to evaluate clinical course of disease:	$ 285,600
• Cost for fiber burden & lung dosimetry modeling study:	$1,412,500
• **Previous Funding Total Allocation for J & K:**	**[$1,196,648]**
• Total New Costs for studies under funding needs areas J & K:	$5,321,672
• Total New Costs for RfC development (funding need A):	$ 886,600
Total Estimated New Costs for Libby Epidemiology Action Plan:	**$6,208,272**